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A randomized clinical trial of the Unified Protocol for Transdiagnostic treatment of emotional and gastrointestinal symptoms in patients with irritable bowel syndrome: evaluating efficacy and mechanism of change

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ABSTRACT

Objective: The aim of this randomized controlled trial was to evaluate the efficacy of Unified Protocol (UP) for transdiagnostic treatment of psychological problems, such as anxiety, depression, and stress, and treating the intensity of gastrointestinal symptoms in individuals with Irritable Bowel Syndrome (IBS). Another aim of the study was to test whether emotion regulation mediates the effect of UP.

Methods: Among 91 patients diagnosed with IBS (using ROME III criteria), 64 patients were eligible to participate in the study based on the inclusion/exclusion criteria. These patients were randomly assigned to either an intervention group (n = 32) that participated in 12 weekly UP treatment sessions or to a wait-list control group (n = 32). All patients completed the Depression, Anxiety, and Stress Scale (DASS-42), Emotion Regulation Questionnaire (ERQ), and Gastrointestinal Symptoms Rating Scale (GSRS) pre- and post-intervention. The data were analyzed with SPSS 20.0 software.

Results: The results of intention-to-treat (ITT) analysis indicated a significant decrease in depression, anxiety, stress, and gastrointestinal symptoms, as well as significant improvements in emotion regulation scores in the intervention group post intervention. All results were significant at $P < .001$. Mediation analyses indicated that changes in emotion regulation mediated the effect of UP on changes in emotional and gastrointestinal symptoms.

Conclusion: UP was effective and influential in emotion regulation among the intervention group and caused a decline in emotional and gastrointestinal symptoms. Hence, this intervention is promising, but larger RCTs are needed to more investigate its efficacy. Future studies could also examine the efficacy of the UP in other medical conditions with co-occurring psychological conditions.

The study is registered at the irct.ir database under registration number IRCT2017010431765N1.

1. Introduction

Irritable bowel syndrome (IBS) is the most prevalent functional gastrointestinal disorder, affecting 10%–22% of the adult population [1]. IBS is characterized by abdominal discomfort, changes in bowel habits, and pain without any structural abnormalities. Since there are no clear-cut diagnostic signs of IBS, its diagnosis is based on clinical manifestations [2]. This syndrome is widespread among all countries and socio-economic classes, and it is more prevalent among women than men [3]. Indirect effects of IBS include social isolation, employee absenteeism, and financial problems, and it may put undue financial pressure on the society's economy [4]. In Iran, the overall incidence of IBS has been reported to be between 1.1% and 25% [5].

Many studies have confirmed that various psychological disorders are widely prevalent among patients with IBS [6, 7]. IBS is more closely associated with anxiety and depression than with other psychiatric disorders [8]. It has been reported that patients IBS suffer from generalized anxiety disorder, depression, or panic disorder [9, 10]. Psychological comorbidities, especially depression and anxiety in IBS, are correlated with personal suffering, decreased social functioning, reduced treatment adherence, poor quality of life [11].

Moreover, patients with depression and anxiety may apply inefficient or passive coping skills for emotion regulation [12]. Previous studies have indicated that many patients with IBS suffer from emotion dysregulation and are not able to identify and express their emotions may be at risk of somatoform disorders and may have more intense physical symptoms, as they are unable to distinguish emotions from physical states [13].

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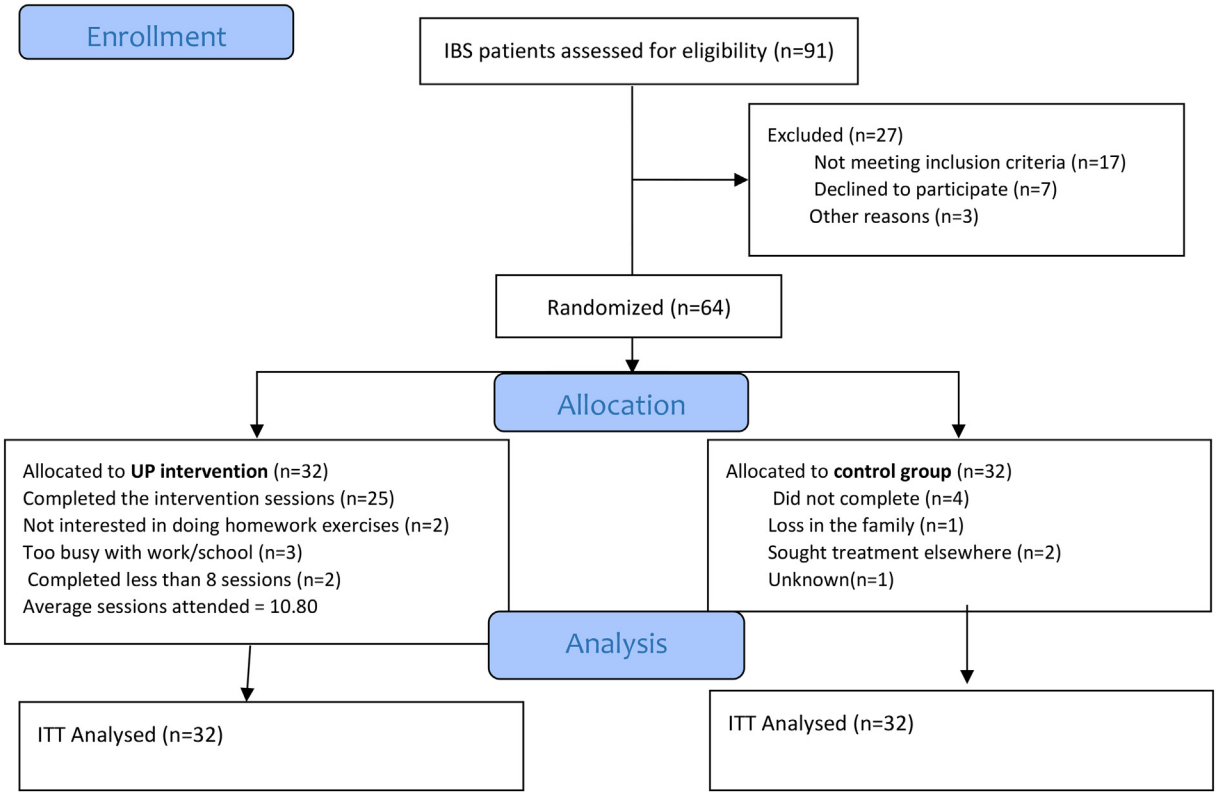

Fig. 1. Flow diagram of the study
Note: ITT = intention-to-treat.

Pharmacological and psychological treatments have both been shown to be effective in reducing the symptoms of IBS, but they have limitations. Pharmacological treatments can temporarily alleviate IBS symptoms [14], they are often expensive and may have negative side effects such as dry eyes, dry mouth, urinary retention, sedation, drowsiness, palpitations, and visual changes, as well as a risk of overdose (whether unintentional or deliberate) and cardiac arrhythmias [15, 16]. On the other hand, the psychological treatments used for IBS include cognitive behavioral therapy (CBT); hypnosis; and mindfulness-based, psychodynamic, and interpersonal therapies [17–19]. Psychological treatment improves physical symptoms severity, depression, and anxiety, overall with small to moderate effect sizes [20]. They involve numerous protocols for targeting specific disorders despite a high rate of comorbidity in patients.

To improve treatment, integrative treatments are recommended. The Unified Protocol for the transdiagnostic treatment of emotional disorders focuses on targeting emotional dysregulation as a common maladaptive coping strategy across different emotional disorders. UP is a cognitive behavioral intervention including 5 core components that target temperamental features, especially neuroticism and resulting emotion dysregulation, underlying all depressive, anxiety and associated disorders [21]. In a systematic review, improvements in emotional regulation was associated with improvements in depression and anxiety [22]. Various researches have examined the efficacy of transdiagnostic treatments in comorbid emotional disorders and improving the emotion regulation of patients with comorbid anxiety and depression [23–26].

The reasons for examining the usage of UP for the treatment of IBS include the high frequency of emotional disorders comorbidities in IBS and the efficacy of UP in targeting emotion regulation through emotional exposure and skills training. Consequently, the purpose of this paper is twofold: 1) examining the efficacy of UP in treating psychological problems such as anxiety, depression, and stress in patients suffering from IBS and 2) examining the mediating role of emotion regulation in relationship between UP and reduce emotional disorder and IBS symptom severity.

2. Methods

This study was a parallel-group randomized clinical trial with intervention and waitlist control group to assess the efficacy of the UP in patients with IBS. The population consisted of all patients with IBS in Shahid Beheshti Hospital of Kashan who referred to the hospital in 2017 and gastroenterology experts confirmed that they had IBS based on **ROME III** criteria. All participants completed the informed consent form. The inclusion criteria consisted of: receiving the diagnosis of IBS based on Rome III criteria, 18–40 age range, Having emotional symptoms based on cut-off-score ≥ 15 in the depression and anxiety subscale of DASS-42, having at least a high school degree (because the UP required activity of individuals, and they had to do some assignment at home which needed their motivation, vigor, and their ability in identifying thoughts and emotions), to be willing and consent for participating in the study. Exclusion criteria consisted of: receiving other psychological treatments since last year and during the research process, having bowel surgery, psychotic characteristics or suicidal thoughts, organic mental disorder, history of drug abuse or drug dependence.

The present study was approved by the ethics committee of Kashan University of Medical Science with the number of IR.KAUMS.REC.1395.100. Written informed consents obtained from all participants. The study is registered at the irct.ir database under registration number IRCT2017010431765N1.

2.1. Participants

Among 91 patients with IBS who referred to the Shahid Beheshti

Table 1
Description of the components of the UP in the intervention group.

Components	Session
1. Motivation enhancement	1
2. Psychoeducational and treatment rationale	2
3. Emotion awareness training	3–4
4. Cognitive reappraisal	5
5. Emotion avoidance	6
6. Emotion-driven behaviors and emotional avoidance	7
7. Awareness and tolerance of physical sensations	8
8. Interoceptive and situational exposure	9–11
9. Relapse prevention	12

Hospital of Kashan in 2017, 64 individuals identified as eligible according to inclusion and exclusion criteria (Fig.1). Participants were randomly assigned to the wait-list control and intervention group by using a random number table. They were asked not to make any changes in their medication during the study. The intervention group received 12 weekly sessions of UP treatment which each session lasted 2 h.

Recruitment for the study started in July 2017 and ended in October 2017. All participants completed the assessments prior to the intervention and immediately following the final visit.The evaluators and analysts were blinded to randomize assignment.

2.2. Intervention protocol

The intervention was based on Barlow et al. protocol [27]. The aim of UP is to foster emotional regulation by cultivating the 5 core processes of UP, including: 1) to increase emotional awareness at the present moment, 2) cognitive flexibility, 3) to prevent maladaptive emotion-driven behaviors and emotional avoidance, 4) to increase awareness and tolerance of physical sensations, and 5) to practice interoceptive and situational exposure (Table 1).

2.3. Therapists and treatment integrity

UP treatment was run by an MSc in clinical psychology with three years of therapy experience and one PhD in clinical psychology with 6 years of experience. Treatment adherence was monitored weekly by a supervisor with PhD. of clinical psychology who was also certified in the UP. Supervisor used the Therapist Adherence Rating Scale (Barlow, personal communication, 2017) as a fidelity form.

2.4. Control condition

The wait-list control group in this study received no psychological treatment, but all study participants received their usual pharmaceutical treatment (See Table 2). The wait-list control group received written information about the causes, symptoms of IBS, an explanation of how IBS is diagnosed, and diets associated with IBS. UP treatment was offered to the wait-list control group after the end of the study.

3. Measurements

3.1. Depression, anxiety and stress scale (DASS-42)

This 42-item scale is a self-report instrument that developed by Lovibond and Lovibond [28]. Items are rated on a four-point scale (ranged from 0 to 3) and reflect the frequency and severity of emotional experiences over the last week. The DASS assess the severity of three psychological conditions of anxiety, depression, and stress. Studies reported good validity and reliability for DASS-42 [28]. It demonstrated good reliability in the current study (Cronbach's $\alpha = 0.87$ for depression subscale; $\alpha = 0.82$ for anxiety subscale; $\alpha = 0.78$ for stress subscale).

Table 2
Participants' characteristics of intent-to-treat sample for each group at baseline.

Variables	Study participants			
	All (n = 64)	UP (n = 32)	control (n = 32)	*P*- Value
Age, mean (± SD)	30.9(± 5.2)	31.2(± 4.7)	30.6(± 5.7)	.68[a]
Sex, n (%)				
Male	26(40.6)	12(37)	14(44)	.61[b]
Female	38(59.4)	20(63)	18(56)	
Marital status, n (%)				
Single	21(32.8)	10(31)	11(34)	.79[b]
Married	43(67.2)	22(69)	21(66)	
Education, n (%)				
High school	28(43.8)	15(47)	13(41)	.85[b]
Bachelor"s degree	21(32.8)	9(28)	12(38)	
Master"s degree	10(15.6)	5(16)	5(16)	
Ph.D.	5(7.8)	3(9)	2(6)	
Disease duration, mean (± SD)	6.1(± 1.9)	6.2(± 1.9)	6.0(± 1.9)	.61[a]
Drug utilization, n (%)				
Anticholinergics	18(24.7)	8(21.6)	10(27.8)	.15[b]
Antispasmodics	18(24.7)	9(24.3)	9(25)	
Antidepressants	6(8.2)	3(8.1)	3(8.3)	
Antinauseants	7(9.6)	4(10.8)	3(8.3)	
Antibiotics	5(6.8)	3(8.1)	2(5.6)	
Laxatives	13(17.8)	7(18.9)	6(16.7)	
Antidiarrheal agents	6(8.2)	3(8.1)	3(8.3)	
Psychosocial characteristics				
Depression (DASS-42)	23.8(5.8)	23.7(6.4)	23.8(5.2)	.93[a]
Anxiety (DASS-42)	21.7(6.3)	21.5(6.3)	22.0(6.5)	.72[a]
Stress (DASS-42)	24.6(3.7)	24.9(3.4)	24.4(4.1)	.64[a]
Cognitive reappraisal(ERQ)	14.5(4.6)	14.0(4.4)	15.0(4.9)	.39[a]
Expressive suppression (ERQ)	19.0(3.3)	19(3.5)	19.1(3.2)	.88[a]
Symptom severity (GSRS)	55.3(6.9)	54(7.2)	56.6(6.5)	.13[a]

P = P value; SD = Standard deviation.
[a] Independent samples t-test.
[b] Chi-square test.

3.2. Emotion regulation questionnaire (ERQ)

This questionnaire was developed by Gross and John [29] to measure emotion regulation strategies. This scale is made up of 10 items consisting of 4 suppression items and 6 reappraisal ones. Each item must be answered on a 7- point scale ranging from 1 (strongly disagree) to 7 (strongly agree). The reliability and validity of the ERQ have been confirmed [29]. This scale demonstrated good reliability in the current study (Cronbach's $\alpha = 0.94$ for reappraisal subscale and 0.89 for suppression).

3.3. Gastrointestinal symptoms rating scale (GSRS)

This scale is made up of 15 questions combined in to 5 symptom clusters which depict the most common signs of gastrointestinal disorders. These questions assess the severity of gastrointestinal symptoms based of a 7 -point Likert scale ranging from (1) means no discomfort to (7) means very severe discomfort. Higher values indicate the severity of symptoms [30]. The GSRS shown good reliability in the current study (Cronbach's $\alpha = 0.82$).

3.4. Statistical analysis

Kolmogorov–Smirnov test and Levene's test were used to determine normality and equality of variance. Chi-square test and independent *t*-test were used for examination of differences between groups in demographic characteristics. The analyses were based on the intention-to-treat principle (ITT). Data analyses of primary and secondary outcomes were conducted using linear mixed models (LMMs). LMMs analyses were utilized to examine time × group and main time and group effects between the UP and wait-list groups on outcome measures at pre-treatment and post-treatment. Time, condition, and a time × condition were considered as fixed effects and participant identifier was considered as a random effect, allowing for participant intercepts to vary by individual and model run with unstructured covariance type. All available data were used because fitting linear mixed models does not require imputation of missing data. Dropping data were handled using the last observation-carried-forward (LOCF) method. Estimates from the LMMs analyses were also used to calculate treatment effect sizes from pre to post treatment. Also, Effect sizes for UP versus WLC mean using Cohen's d were calculated using the difference between two means divided by a standard deviation for the data [31]. The mediation analysis was tested by multiple regression analyses, controlling for age, sex and education. Sobel test was calculated to test significance of the mediation effect [32]. The data were analyzed using Statistical Package for the Social Sciences version 20.0 (SPSS Inc., Chicago, IL, USA) and a $P < .05$ considered as statistically significant.

4. Results

4.1. Participants' characteristics

Fig. 1 is illustrating CONSORT diagram of participant flow during the study. According to Figs. 1, 64 patients were eligible regarding inclusion/exclusion criteria (rate of eligibility: 64/91 = 70%). Seven patients dropped out of the intervention group (dropout rate 7/32 = 22%) and 4 patients dropped out of the wait-listed control condition (dropout rate 4/32 = 13%; adherence rate 53/64 = 83%). Patients that completed the intervention group (n = 25) attended an average of 10.80 (SD = 0.81) out of the sessions.

The demographic characteristics of the participants are presented in Table 2. No significant difference was observed between two groups for any demographic variables, indicating that randomization was successful. The mean age of participants was 30.9 ± 5.2, and 59.4% participants were female. The most of patients were married (n = 43) and 21 of them were single. Most of them had a high school or bachelor degree. The mean diseases duration was 6.1 (SD = 1.9) years among all participants. According to cutoff values on the DASS-42 [28], participants had severe depressive symptoms (mean = 23.8 > 21), extremely severe anxiety (mean = 21.7 > 20), and moderate stress (between19–25; mean = 24.6). There were no significant differences between the intervention and wait-list control groups regarding drug therapy ($\chi^2 = 21.77$; p = .15) (See Table 2).

4.2. Effects of treatment on primary treatment outcomes

4.2.1. Depression

The LMMs analysis of the depression scores demonstrated a significant time × group interaction, F(1, 99.350) = 15.15, p < .001. Between group comparisons indicated significant differences between the treatment conditions at post-treatment t(62) = 2.644, p < .01, d = 1.23. Within-group comparisons indicated a significant difference for the UP condition from pre- to post-treatment t(31) = 6.33, p < .001, d = 1.01. Significant differences were not found for the wait-list condition from pre- to post-treatment t(31) = 0.424, p = .674, d = 0.05. These findings indicated that treatment UP had a large, significant impact on reducing depression over the treatment period

Table 3
Results linear mixed models for depression, anxiety, stress, emotion regulation and symptoms severity.

	Mean (± SD)				Cohen's d	Results linear mixed models		
	Up(n = 32)		Control(n = 32)					
Primary outcomes	Pre-test	Post-test	Pre-test	Post-test	UP vs WLC (95% CI)	Group	Time	Time x Group
Depression	23.75(± 6.41)	17.31(± 6.27)	23.88(± 5.26)	23.59(± 5.08)	1.23(0.57–1.62)	F (1, 62) = 6.98, p < .01	F(1, 99.350) = 18.04, p < .001	F(1, 99.350) = 15.15, p < .001
Anxiety	21.50(± 6.32)	14.44(± 5.55)	22.06(± 6.55)	21.28(± 7)	0.97(0.55–1.60)	F(1, 62) = 5.95, p < .01	F(1, 105.01) = 22.16, p < .001	F(1, 105.01) = 14.21, p < .001
Stress	24.91(± 3.43)	20.09(± 4.78)	24.47(± 4.12)	24.84(± 4.58)	1.03(0.49–1.53)	F(1, 62) = 15.45, p < .001	F(1, 111.88) = 17.75, p < .001	F(1, 111.88) = 24.26, p < .001
Symptom severity purported mediator emotion regulation	54(± 7.26)	46.25(± 8.21)	56.63(± 6.57)	54.88(± 6.48)	1.33(0.63–1.69)	F(1, 62) = 4.29, p < .02	F(1, 95.460) = 21.98, p < .001	F(1, 95.460) = 8.77, p < .004
-Cognitive reappraisal	14.09(± 4.47)	21.34(± 6.18)	15.09(± 4.93)	14.75(± 4.98)	1.32(1.70–0.64)	F(1, 62) = 22.80, p < .001	F(1, 109.33) = 27.95, p < .001	F(1, 109.33) = 33.79, p < .001
-Suppression	19(± 3.57)	15.34(± 4.34)	19.13(± 3.26)	18.81(± 3.31)	1.04(0.38–1.41)	F(1, 62) = 5.74, p < .02	F(1, 104.79) = 17.32, p < .001	F(1, 104.79) = 12.29, p < .001

Note: ITT: intent-to-treat; Depression: Depression, Anxiety and Stress Scale (DASS-42); Anxiety: DASS-42; Stress: DASS-42; Cognitive Reappraisal: Emotion Regulation Questionnaire; Expressive Suppression: Emotion Regulation Questionnaire; Symptom severity: Gastrointestinal Symptoms Rating Scale.

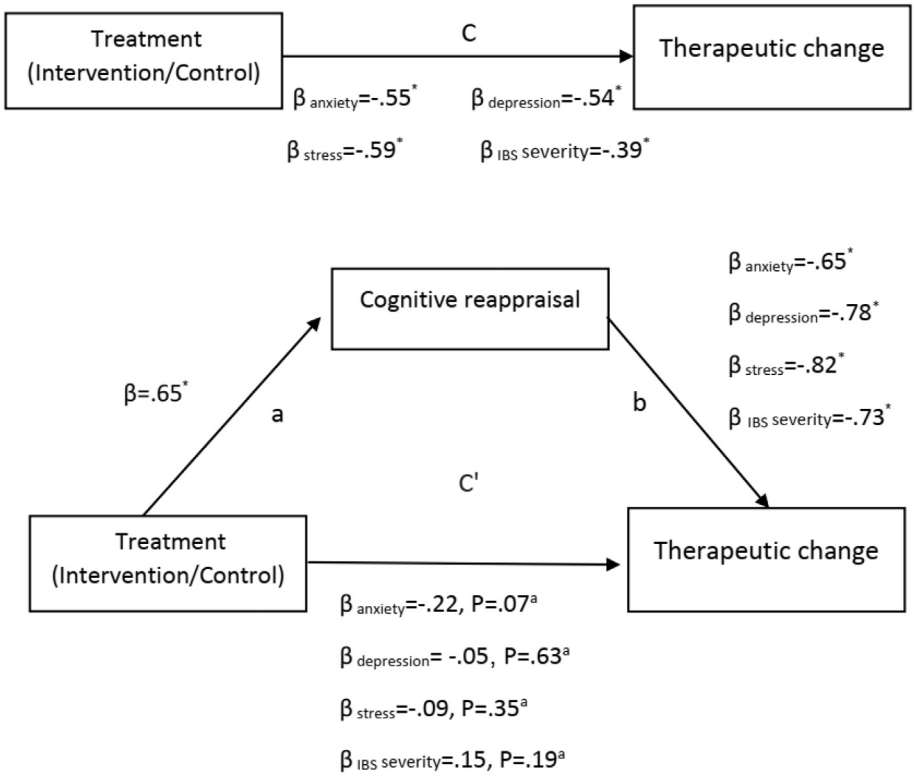

Fig. 2. Direct and Indirect effects of UP on change in emotional (stress, anxiety, and depression) and gastrointestinal symptoms from pre to post-intervention via change in the cognitive reappraisal.
Notes $_{*}p < 0.05$; a: Full Mediation (a relationship between independent and dependent variable (C) that was initially significant has to become insignificant in the presence of the mediator (C′).
Model covariates: age, sex and education.

Table 3.

4.2.2. Anxiety

The analysis of the anxiety scores revealed a significant time × group interaction, $F(1, 105.01) = 14.21$, $p < .001$. Between group comparisons indicated significant differences between the treatment conditions at post-treatment $t(62) = 2.440$, $p < .01$, $d = 0.97$. Within-group comparisons indicated a significant difference for the UP condition from pre- to post-treatment $t(31) = 7.295$, $p < .001$, $d = 1.18$. Significant differences were not found for the wait-list condition from pre- to post-treatment $t(31) = 1.143$, $p = .26$, $d = 0.11$. These findings indicated that treatment UP had a large, significant impact on reducing anxiety in patients suffering from IBS.

4.2.3. Stress

The LMMs analysis of the stress scores revealed a significant time × group interaction, $F(1, 111.01) = 24.26$, $p < .001$. Between group comparisons indicated significant differences between the treatment conditions at post-treatment $t(62) = 3.931$, $p < .001$, $d = 1.03$. Within-group comparisons indicated a significant difference for the UP condition from pre- to post-treatment $t(31) = 7.706$, $p < .001$, $d = 1.15$, but not for the wait-list condition $t(31) = -0.579$, $p = .56$, $d = 0.08$. These findings indicated that treatment UP had a large, significant impact on reducing stress in patients with IBS.

4.2.4. Symptom severity

Symptom severity scores revealed a significant time × group interaction, $F(1, 95.460) = 8.77$, $p < .004$. Between group comparisons indicated significant differences between the treatment conditions at post-treatment $t(62) = 2.96$, $p < .02$, $d = 1.33$. Within-group comparisons indicated a significant difference for the UP condition from pre- to post-treatment $t(31) = 6.016$, $p < .001$, $d = 1$. Significant differences were not found for the wait-list condition from pre- to post-treatment $t(31) = 1.44$, $p = .15$, $d = 0.26$. These findings indicated that treatment UP had a large, significant impact on reducing symptom severity over the treatment period.

4.3. Effects of treatment on the proposed mediators

4.3.1. Cognitive reappraisal

The LMMs analysis of the cognitive reappraisal scores demonstrated a significant time × group interaction, $F(1, 109.33) = 33.79$, $p < .001$. Between group comparisons indicated significant differences between the treatment conditions at post-treatment $t(62) = -4.776$, $p < .001$, $d = 1.32$. Within-group comparisons indicated a significant difference for the UP condition from pre- to post-treatment $t(31) = -7.199$, $p < .001$, $d = 1.34$. Significant differences were not found for the wait-list condition from pre- to post-treatment $t(31) = -0.756$, $p = .455$, $d = 0.06$. These findings indicated that treatment UP had a large, significant impact on improving cognitive reappraisal over the treatment period.

4.3.2. Suppression

Suppression scores demonstrated a significant time × group interaction, $F(1, 104.79) = 12.29$, $p < .001$. Between group comparisons indicated significant differences between the treatment conditions at post-treatment $t(62) = 2.39$, $p < .02$, $d = 1.04$. Within-group comparisons indicated a significant difference for the UP condition from pre- to post-treatment $t(31) = 5.175$, $p < .001$, $d = 0.92$. Significant differences were not found for the wait-list condition from pre- to post-treatment $t(31) = 0.848$, $p = .40$, $d = 0.09$. These findings indicated that UP had a large impact on reducing suppression in patients with IBS over the treatment period.

4.4. Mediation analyses

The effects of UP on depression, anxiety and stress through changes in emotion regulation was tested based on Baron and Kenny approach [33]. Baron and Kenny (1986) proposed a four-step approach by several regression analyses. 1) The treatment groups should predict therapeutic change (Path C). 2) The treatment groups should predict change in the mediator (Path a). 3) Change in the mediator should predict therapeutic change (Path b). 4) The effect of treatment groups on change in the

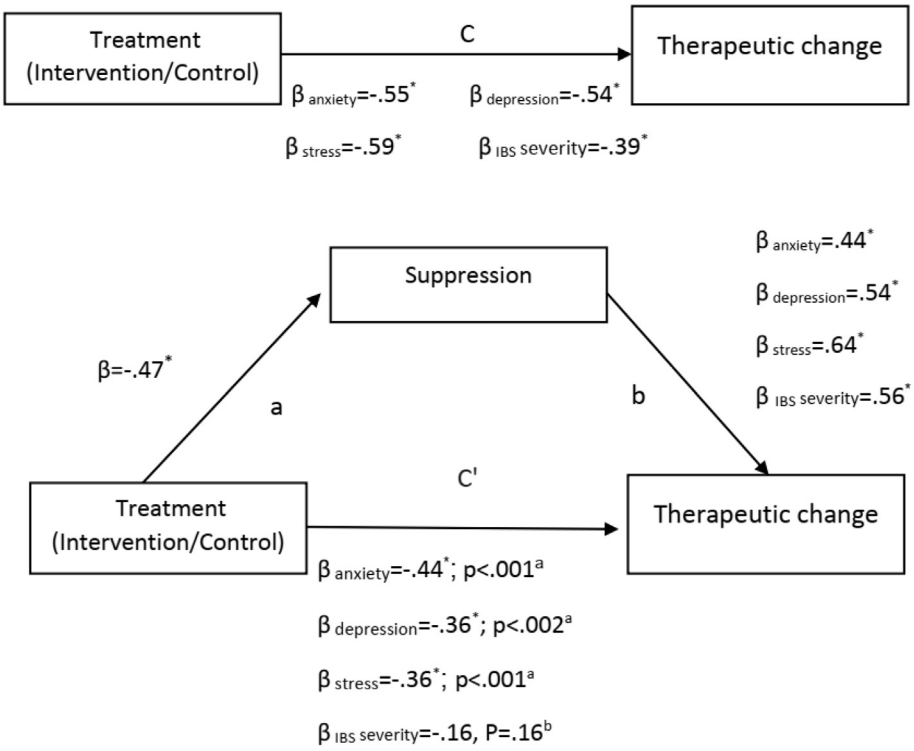

Fig. 3. Direct and Indirect effects of UP on change in emotional (stress, anxiety, and depression) and gastrointestinal symptoms from pre- to post-intervention via change in the suppression.
Notes * P < 0.05; a: Partial mediation (implies that a relationship that was initially significant in the absence of mediator continues to be significant even in the presence of the mediator); b: Full Mediation (a relationship between independent and dependent variable (C) that was initially significant has to become insignificant in the presence of the mediator (C′).
Model covariates: age, sex and education.

outcome should be decreased when change in the mediator is controlled (Path C′). Change scores for each of mediator and outcomes variables demonstrated the difference between the score at posttest and pretest. And treatment groups were TAU (coded 1) and UP (coded 2) consequently, separate linear regression analyses were used to examine mediating role of emotion regulation (Figs. 2 and 3).

4.4.1. Emotion regulation as mediator of treatment outcome

Results of the mediation analyses were presented in Figs. 2 and 3. In both models age, sex and education were controlled as covariates. In the mediation model assessing the role of the cognitive reappraisal in mediating the relationship between UP and therapeutic change, there was a significant indirect effect (Fig. 2). The results indicated full mediation, as the direct effect between UP and therapeutic change was no significant when accounting for the cognitive reappraisal. Similarly, the mediation model 2 assessing the suppression as a mediator indicated suppression fully mediated the relationship between UP and gastrointestinal symptoms change. However, the UP direct effect on the emotional disorders decreased but yet was significant when including the suppression in the model, indicating partial mediation (Fig. 3). Consequently, the Sobel test was used to examine whether this decrease is significant. The Sobel test for this mediation model showed suppression having a significant mediating effect between treatment condition and emotional symptoms ($Z = -3.25$, $P < .001$ for depression, $Z = -2.88$, $P < .003$ for anxiety, $Z = -3.56$, $P < .001$ for stress). These results indicated that change in emotion regulation mediated the effect of UP on change in emotional symptoms and gastrointestinal symptoms severity.

5. Discussion

The main purpose of this study was to investigate the efficacy of UP on anxiety, depression, stress, emotion regulation, and IBS symptoms. The obtained results revealed that UP was beneficial for patients with IBS and could decrease anxiety, depression, stress, and gastrointestinal symptoms in addition to improving emotion regulation. Although only a few studies have been conducted on the effects of UP on patients with IBS, the results of this study were in line with those of research on similar disorders. For instance, our findings are consistent with the results of previous research on the efficacy of UP on the emotional problems of patients with functional gastrointestinal disorders and psychosomatic patients [34]. Furthermore, the results of the present study indicated that UP could be effective in reducing gastrointestinal symptoms. This result was consistent with Johary's study about decreasing IBS symptoms via UP [35]. Previous research has reported the effects of UP on emotional disorders [23, 36–41].

A component of UP considered in this paper is interoceptive exposure. Patients suffering from IBS are more sensitive to visceral sensations than healthy individuals [42, 43]. Visceral sensitivity, which is highly associated with severe IBS symptoms, anxiety, and depression [44–46], is common among IBS patients [47]. According to previous research, visceral sensitivity mediated between gastrointestinal symptoms, anxiety, and neuroticism [45, 46], and the mediating role of visceral senses may improve the results of IBS treatments [48]. Patients with IBS may benefit from interventions that aim at intermediary psychological procedures, including visceral sensitivity [49]. Accordingly, interoceptive exposure has been confirmed to be effective in visceral sensitivity reduction for IBS treatment [48, 50]. Therefore, UP treatment with interoceptive exposure can have an effect on the severity of IBS symptoms, anxiety, depression, and stress.

Another purpose of the study was to investigate whether emotion regulation mediates the effect of UP on changes in emotional and gastrointestinal symptoms in patients with IBS. The results indicated the cognitive reappraisal fully mediated effect UP on the therapeutic change in all of the emotional (stress, anxiety, and depression) and gastrointestinal symptoms. According to results, the suppression partially (not fully) mediated effect of UP on changes in emotional symptoms but fully mediated the relationship between UP and gastrointestinal symptoms change. This study found that UP improved both cognitive reappraisal and expressive suppression that the latter appeared to be more relevant in mediating the effects of UP on psychological and gastrointestinal outcomes in IBS. It seems that UP help IBS patients to identify and express their emotions and it leads them to have less intense psychological and physical symptoms. Results of the

mediation analyses were consistent with the literature, which suggests that emotion regulation is an important construct in the psychopathology and IBS [13, 44]. Research showed that difficulties with emotion regulation are fundamental to the growth and maintenance of psychopathology [51, 52]. It was found that the maladaptive strategies (e.g., suppression and avoidance) to regulate emotion were associated with a wide range of emotional disorders and is directly related to anxiety and depression [53]. It can be concluded that emotion dysregulation is an important factor of the development of psychological disorders in individuals with IBS. In fact, in the majority of psychological disorders, there is at least one symptom of emotional disturbance [54].

The UP particularly targets deficits in emotion regulation and lead to the choice of more adaptive emotion regulation techniques both through skills practice and emotion exposures. The goal of UP is to reduce co-occurring emotional disorders by improved emotion regulation [27]. The present study results provided the support for UP model.

Emotional awareness (EA) as the first step in the process of emotion regulation is correlated with a range of emotional disorders. Patients with psychosomatic disorders, especially IBS, have lower EA or suppress their emotion [55]. EA as a component of UP enables the individual to distinguish between various thoughts, physical sensations, and behaviors that influence their discomfort [15]. Research indicated that EA improved the results of medical treatment of IBS [56]. The purpose of this component is identifying an individual's method of reacting and responding to their emotions, promoting nonjudgmental awareness, and encouraging individuals to concentrate on the present moment via mindfulness skills. Mindfulness allows the individual to distinguish between various thoughts, physical sensations, and behaviors that influence their discomfort [15].Research has indicated that adding EA training to medical treatments may lead to superior results among patients with IBS [56], including a substantial decrease in symptoms and an improved quality of life. Consequently, it seems that UP can decrease the effects of emotional disturbances and ameliorate gastrointestinal symptoms by increasing EA through emotion regulation skills.

In addition to EA, another component of UP is cognitive reappraisal. Cognitive reappraisal is a main emotion regulation strategy [55]. The importance of cognitive appraisal and flexibility for treating patients with IBS has been verified in previous studies [57]. Among patients with IBS, a positive relationship has been traced between cognitive appraisal and abdominal pain and discomfort [58]. Anxiety is also associated with cognitive appraisal among these patients [59]. In one study [60], catastrophizing as a cognitive appraisal had a direct relationship with the severity of participants' IBS symptoms, and it mediated the relationship between anxiety and symptom severity in patients with IBS. In this regard, emphasis on reducing catastrophizing may produce positive results in IBS treatment [61]. Hence, UP is effective in the cognitive appraisal by improving emotion regulation skills which, in turn, leads to decreased emotional symptoms of patients with IBS.

In summary, emotional regulation mediated the improvements in both emotional and gastrointestinal symptoms. This is important and suggests that targeting this common mechanism can be valuable for patients with co-occurring physical and emotional symptoms.

5.1. Limitations and suggestions for future research

There are several limitations in this study. First, the sample size was small, which makes it difficult to generalize the results. Second, the study did not include a follow-up with participants to examine the continuation of the intervention efficacy. Third, the study lacked an “active comparison” group. Fourth, the p-value that is derived from the Sobel test in smaller sample sizes will not be an accurate estimate of the true p-value.

For future research, it is recommended that a similar study be conducted that includes a follow-up stage. An active or CBT group could also be added for comparison with the group receiving UP for treatment. Researchers could investigate which of the UP modules is most clinically effective in treating patients suffering from gastrointestinal diseases.

6. Conclusion

There are several comorbid psychological conditions for patients with IBS, such as anxiety and depression. In this study, UP was used for the transdiagnostic treatment of emotional disorders in individuals with IBS. UP focuses on the common pathologic factors among various diagnostics. The results of the present study confirmed that the UP was efficacious for improving emotion regulation; it helped participants deal with emotional problems and caused a reduction in gastrointestinal symptoms related to IBS. Hence, this protocol can be applied as a complementary treatment to other pharmacotherapies and medical treatments for patients with IBS.

Conflict of interests

Authors have no conflict of interests.

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References

[1] J.J. Heidelbaugh, M. Stelwagon, S.A. Miller, E.P. Shea, W.D. Chey, The spectrum of constipation-predominant irritable bowel syndrome and chronic idiopathic constipation: US survey assessing symptoms, care seeking, and disease burden, Am. J. Gastroenterol. 110 (2015) 580.
[2] G.F. Longstreth, W.G. Thompson, W.D. Chey, L.A. Houghton, F. Mearin, R.C. Spiller, Functional bowel disorders, Gastroenterology 130 (2006) 1480–1491.
[3] J.M. Lackner, R. Gellman, G. Gudleski, K. Sanders, S. Krasner, L. Katz, E.B. Blanchard, Dysfunctional attitudes, gender, and psychopathology as predictors of pain affect in patients with irritable bowel syndrome, J. Cogn. Psychother. 19 (2005) 151–161.
[4] O.Y. Lee, E.A. Mayer, M. Schmulson, L. Chang, B. Naliboff, Gender-related differences in IBS symptoms, Am. J. Gastroenterol. 96 (2001) 2184.
[5] P. Jahangiri, M.S.H. Jazi, A.H. Keshteli, S. Sadeghpour, E. Amini, P. Adibi, Irritable bowel syndrome in Iran: Sepahan systematic review no. 1, Int. J. Prev. Med. 3 (2012) S1–S9.
[6] W.E. Whitehead, O. Palsson, K.R. Jones, Systematic review of the comorbidity of irritable bowel syndrome with other disorders: what are the causes and implications? Gastroenterology 122 (2002) 1140–1156.
[7] D.G. Folks, The interface of psychiatry and irritable bowel syndrome, Curr. Psychiatry Rep. 6 (2004) 210–215.
[8] I. Posserud, J. Svedlund, J. Wallin, M. Simrén, Hypervigilance in irritable bowel syndrome compared with organic gastrointestinal disease, J. Psychosom. Res. 66 (2009) 399–405.
[9] B. Ljótsson, L. Falk, A.W. Vesterlund, E. Hedman, P. Lindfors, C. Rück, T. Hursti, S. Andréewitch, L. Jansson, N. Lindefors, Internet-delivered exposure and mindfulness based therapy for irritable bowel syndrome–a randomized controlled trial, Behav. Res. Ther. 48 (2010) 531–539.
[10] N. Ebrahimidaryani, F. Faramarzigarousi, H. Ghofrani, P. Hosseini, M. Bashashati, A. Asadhashtroudi, Clinical manifestations of irritable bowel syndrome in Iranian men and women: a comparative study, Govaresh. 11 (2006) 17–21.
[11] J. Prasko, D. Jelenova, V. Mihal, Psychological aspects and psychotherapy of inflammatory bowel diseases and irritable bowel syndrome in children, Biomed. Pap. Med. Fac. Univ. Palacky Olomouc Czech Repub. 154 (2010) 307–314.
[12] C. Crane, M. Martin, Social learning, affective state and passive coping in irritable bowel syndrome and inflammatory bowel disease, Gen. Hosp. Psychiatry 26 (2004) 50–58.
[13] K. Sayar, M. Solmaz, S. Trablus, M. Ozturk, B. Acar, Alexithymia in irritable bowel syndrome, Turk. J. Psychiatry 11 (2000) 190–197.
[14] M. Camilleri, A.C. Ford, Pharmacotherapy for irritable bowel syndrome, J. Clin. Med. 6 (2017) 101.
[15] S.A. Gaylord, O.S. Palsson, E.L. Garland, K.R. Faurot, R.S. Coble, J.D. Mann, W. Frey, K. Leniek, W.E. Whitehead, Mindfulness training reduces the severity of irritable bowel syndrome in women: results of a randomized controlled trial, Am. J. Gastroenterol. 106 (2011) 1678–1688.

[16] B.E. Lacy, K. Weiser, R. De Lee, The treatment of irritable bowel syndrome, Therap. Adv. Gastroenterol. 2 (2009) 221–238.
[17] T. Hyphantis, E. Guthrie, B. Tomenson, F. Creed, Psychodynamic interpersonal therapy and improvement in interpersonal difficulties in people with severe irritable bowel syndrome, Pain 145 (2009) 196–203, https://doi.org/10.1016/j.pain.2009.07.005.
[18] A.C. Ford, E.M.M. Quigley, B.E. Lacy, A.J. Lembo, Y.A. Saito, L.R. Schiller, E.E. Soffer, B.M.R. Spiegel, P. Moayyedi, Effect of antidepressants and psychological therapies, including hypnotherapy, in irritable bowel syndrome: systematic review and meta-analysis, Am. J. Gastroenterol. 109 (2014) 1350.
[19] S. Ballou, L. Keefer, Psychological interventions for irritable bowel syndrome and inflammatory bowel diseases, Clin. Transl. Gastroenterol. 8 (2017) e214.
[20] A. Martin, M. Härter, P. Henningsen, W. Hiller, B. Kröner-Herwig, W. Rief, Evidenzbasierte Leitlinie zur Psychotherapie somatoformer Störungen und assoziierter Syndrome, Hogrefe Verlag, 2013.
[21] D.H. Barlow, S. Sauer-Zavala, J.R. Carl, J.R. Bullis, K.K. Ellard, The nature, diagnosis, and treatment of neuroticism: Back to the future, Clin. Psychol. Sci. 2 (2014) 344–365.
[22] E. Sloan, K. Hall, R. Moulding, S. Bryce, H. Mildred, P.K. Staiger, Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating and borderline personality disorders: A systematic review, Clin. Psychol. Rev. 57 (2017) 141–163.
[23] M. Ito, M. Horikoshi, N. Kato, Y. Oe, H. Fujisato, S. Nakajima, A. Kanie, M. Miyamae, Y. Takebayashi, R. Horita, M. Usuki, A. Nakagawa, Y. Ono, Transdiagnostic and Transcultural: Pilot Study of Unified Protocol for Depressive and Anxiety Disorders in Japan, Behav. Ther. 47 (2016) 416–430, https://doi.org/10.1016/j.beth.2016.02.005.
[24] K.K. Ellard, C.P. Fairholme, C.L. Boisseau, T.J. Farchione, D.H. Barlow, Unified protocol for the transdiagnostic treatment of emotional disorders: Protocol development and initial outcome data, Cogn. Behav. Pract. 17 (2010) 88–101.
[25] K.K. Ellard, T. Deckersbach, L.G. Sylvia, A.A. Nierenberg, D.H. Barlow, Transdiagnostic treatment of bipolar disorder and comorbid anxiety with the unified protocol: a clinical replication series, Behav. Modif. 36 (2012) 482–508.
[26] T.J. Farchione, C.P. Fairholme, K.K. Ellard, C.L. Boisseau, J. Thompson-Hollands, J.R. Carl, M.W. Gallagher, D.H. Barlow, Unified protocol for transdiagnostic treatment of emotional disorders: a randomized controlled trial, Behav. Ther. 43 (2012) 666–678.
[27] D.H. Barlow, T.J. Farchione, S. Sauer-Zavala, H.M. Latin, K.K. Ellard, J.R. Bullis, K.H. Bentley, H.T. Boettcher, C. Cassiello-Robbins, Unified Protocol for Transdiagnostic Treatment of Emotional Disorders: Therapist Guide, Oxford University Press, 2011.
[28] P.F. Lovibond, S.H. Lovibond, The structure of negative emotional states: Comparison of the Depression Anxiety Stress Scales (DASS) with the Beck Depression and Anxiety Inventories, Behav. Res. Ther. 33 (1995) 335–343, https://doi.org/10.1016/0005-7967(94)00075-U.
[29] J.J. Gross, O.P. John, Individual differences in two emotion regulation processes: implications for affect, relationships, and well-being, J. Pers. Soc. Psychol. 85 (2003) 348.
[30] D.A. Revicki, M. Wood, I. Wiklund, J. Crawley, Reliability and validity of the Gastrointestinal Symptom Rating Scale in patients with gastroesophageal reflux disease, Qual. Life Res. 7 (1997) 75–83.
[31] W.P. Dunlap, J.M. Cortina, J.B. Vaslow, M.J. Burke, Meta-analysis of experiments with matched groups or repeated measures designs, Psychol. Methods 1 (1996) 170.
[32] M.E. Sobel, Some new results on indirect effects and their standard errors in covariance structure models, Sociol. Methodol. 16 (1986) 159–186.
[33] R.M. Baron, D.A. Kenny, The moderator–mediator variable distinction in social psychological research: Conceptual, strategic, and statistical considerations, J. Pers. Soc. Psychol. 51 (1986) 1173.
[34] M. Mazaheri, H. Daghaghzadeh, H. Afshar, N. Mohammadi, The effectiveness of the unified protocol on emotional dysregulation and cognitive emotion regulation strategies in patients with psychosomatic disorders, Int. J. Body, Mind Cult. 1 (2013) 73–82.
[35] R. Johari-Fard, R. Ghafourpour, The Effectiveness of Unified Treatment Approach on Quality of Life and Symptoms of Patients with Irritable Bowel Syndrome Referred to Gastrointestinal Clinics, Int. J. Body, Mind Cult. 2 (2015) 85–94.
[36] J.M. Laposa, E. Mancuso, G. Abraham, L. Loli-Dano, Unified Protocol Transdiagnostic Treatment in Group Format: A Preliminary Investigation With Anxious Individuals, Behav. Modif. 41 (2017) 253–268.
[37] C.L. Boisseau, T.J. Farchione, C.P. Fairholme, K.K. Ellard, D.H. Barlow, The development of the unified protocol for the transdiagnostic treatment of emotional disorders: A case study, Cogn. Behav. Pract. 17 (2010) 102–113.
[38] M. Ito, M. Horikoshi, N. Kato, Y. Oe, H. Fujisato, S. Nakajima, A. Kanie, M. Miyamae, Y. Takebayashi, R. Horita, Transdiagnostic and transcultural: pilot study of unified protocol for depressive and anxiety disorders in Japan, Behav. Ther. 47 (2016) 416–430.
[39] J.R. Bullis, S. Sauer-Zavala, K.H. Bentley, J. Thompson-Hollands, J.R. Carl, D.H. Barlow, The unified protocol for transdiagnostic treatment of emotional disorders:preliminary exploration of effectiveness for group delivery, Behav. Modif. 39 (2015) 295–321, https://doi.org/10.1177/0145445514553094.
[40] A.C.C. Maia, A.A. Braga, C.A. Nunes, A.E. Nardi, A.C. Silva, Transdiagnostic treatment using a unified protocol: application for patients with a range of comorbid mood and anxiety disorders, Trends Psychiatr. Psychother. 35 (2013) 134–140.
[41] J.R. Bullis, M.R. Fortune, T.J. Farchione, D.H. Barlow, A preliminary investigation of the long-term outcome of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders, Compr. Psychiatry 55 (2014) 1920–1927, https://doi.org/10.1016/j.comppsych.2014.07.016.
[42] K. Tillisch, J.S. Labus, B.D. Naliboff, R. Bolus, M. Shetzline, E.A. Mayer, L. Chang, Characterization of the alternating bowel habit subtype in patients with irritable bowel syndrome, Am. J. Gastroenterol. 100 (2005) 896–904.
[43] G.N. Verne, M.E. Robinson, D.D. Price, Hypersensitivity to visceral and cutaneous pain in the irritable bowel syndrome, Pain 93 (2001) 7–14.
[44] T. Saigo, J. Tayama, T. Hamaguchi, N. Nakaya, T. Tomiie, P.J. Bernick, M. Kanazawa, J.S. Labus, B.D. Naliboff, S. Shirabe, Gastrointestinal specific anxiety in irritable bowel syndrome: validation of the Japanese version of the visceral sensitivity index for university students, Biopsychosoc. Med. 8 (2014) 10.
[45] J.S. Labus, E.A. Mayer, L. Chang, R. Bolus, B.D. Naliboff, The central role of gastrointestinal-specific anxiety in irritable bowel syndrome: further validation of the visceral sensitivity index, Psychosom. Med. 69 (2007) 89–98.
[46] J.S. Labus, R. Bolus, L. Chang, I. Wiklund, J. Naesdal, E.A. Mayer, B.D. Naliboff, The Visceral Sensitivity Index: development and validation of a gastrointestinal symptom-specific anxiety scale, Aliment. Pharmacol. Ther. 20 (2004) 89–97.
[47] P. Jerndal, G. Ringström, P. Agerforz, M. Karpefors, L.M. Akkermans, A. Bayati, M. Simrén, Gastrointestinal-specific anxiety: an important factor for severity of GI symptoms and quality of life in IBS, Neurogastroenterol. Motil. 22 (2010) 646.
[48] K. Wolitzky-Taylor, M.G. Craske, J.S. Labus, E.A. Mayer, B.D. Naliboff, Visceral sensitivity as a mediator of outcome in the treatment of irritable bowel syndrome, Behav. Res. Ther. 50 (2012) 647–650.
[49] S.R. Knowles, D.W. Austin, S. Sivanesan, J. Tye-Din, C. Leung, J. Wilson, D. Castle, M.A. Kamm, F. Macrae, G. Hebbard, Relations between symptom severity, illness perceptions, visceral sensitivity, coping strategies and well-being in irritable bowel syndrome guided by the common sense model of illness, Psychol. Health Med. 22 (2017) 524–534.
[50] M.G. Craske, K.B. Wolitzky-Taylor, J. Labus, S. Wu, M. Frese, E.A. Mayer, B.D. Naliboff, A cognitive-behavioral treatment for irritable bowel syndrome using interoceptive exposure to visceral sensations, Behav. Res. Ther. 49 (2011) 413–421.
[51] K.L. Gratz, N.H. Weiss, M.T. Tull, Examining emotion regulation as an outcome, mechanism, or target of psychological treatments, Curr. Opin. Psychol. 3 (2015) 85–90.
[52] A. Aldao, K.L. Dixon-Gordon, Broadening the scope of research on emotion regulation strategies and psychopathology, Cogn. Behav. Ther. 43 (2014) 22–33.
[53] A. Aldao, S. Nolen-Hoeksema, S. Schweizer, Emotion-regulation strategies across psychopathology: A meta-analytic review, Clin. Psychol. Rev. 30 (2010) 217–237.
[54] A.M. Kring, D.M. Sloan, Emotion Regulation and Psychopathology: A Transdiagnostic Approach to Etiology and Treatment, Guilford Press, 2009.
[55] J.J. Gross, O.P. John, Mapping the domain of expressivity: multimethod evidence for a hierarchical model, J. Pers. Soc. Psychol. 74 (1998) 170.
[56] A. Farnam, M.H. Somi, S. Farhang, N. Mahdavi, M.A. Besharat, The therapeutic effect of adding emotional awareness training to standard medical treatment for irritable bowel syndrome: a randomized clinical trial, J. Psychiatr. Pract. 20 (2014) 3–11.
[57] M. Ben-Ezra, Y. Hamama-Raz, S. Palgi, Y. Palgi, Cognitive appraisal and psychological distress among patients with irritable bowel syndrome, Isr. J. Psychiatry Relat. Sci. 52 (2015) 54–59.
[58] N. Sugaya, S. Nomura, Relationship between cognitive appraisals of symptoms and negative mood for subtypes of irritable bowel syndrome, Biopsychosoc. Med. 2 (2008) 9.
[59] N. Sugaya, E. Yoshida, S. Yasuda, M. Tochigi, K. Takei, T. Ohtani, T. Otowa, T. Minato, T. Umekage, Y. Sakano, Irritable bowel syndrome, its cognition, anxiety sensitivity, and anticipatory anxiety in panic disorder patients, Psychiatry Clin. Neurosci. 67 (2013) 397–404.
[60] M.A.L. Van Tilburg, O.S. Palsson, W.E. Whitehead, Which psychological factors exacerbate irritable bowel syndrome? Development of a comprehensive model, J. Psychosom. Res. 74 (2013) 486–492.
[61] L.B. Sherwin, E. Leary, W.A. Henderson, The association of catastrophizing with quality-of-life outcomes in patients with irritable bowel syndrome, Qual. Life Res. (2017) 1–10.